14

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20040115

Application Number: 09/508,570
Filing Date: May 23, 2000
Appellant(s): ARMINJON ET AL.

Michael S. Greenfield
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 18, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The brief does not contain a statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Therefore, it is presumed that there are none. The Board, however, may exercise its discretion to require an explicit statement as to the existence of any related appeals and interferences.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 21-27 and 29-38 as obvious under 35 U.S.C. 103(a) stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

WO 93/24148 A1	PETRE *et al.*	9-1993
AU 708777	ARMINJON *et al.*	12-1996
WO 96/37222	ARMINJON *et al.*	11-1996

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 21-27 and 29-38 are rejected under 35 U.S.C. 103(a) as obvious over Petre *et al.* (WO 93/24148 A1) in view of Arminjon *et al.* (AU 708777).

Petre teaches multicomponent vaccines for infants comprising various antigens such as diphtheria, tetanus, pertussis (toxoid and filamentous hemagglutinin), hepatitis B surface antigen (HBsAg), IPV (inactivated polio virus) and HiB (*H. influenzae* type B), (abstract, and page 4, lines 10-36). Petre teaches that the components of the combined vaccine are adsorbed to AH (aluminum hydroxide) or AP (aluminum phosphate). The following excerpt is taken from Petre, "After allowing time for complete and stable adsorption of the respective components, the

different components are combined under appropriate conditions", page 9, lines 1-3 of Petre. Therefore, Petre clearly teaches adsorption prior to mixing with other components. With regard to IPV (inactivated polio virus) which is not adsorbed in the instant claim 23, Petre discloses instances where only one of the components of the multivalent vaccine is adsorbed to an aluminum salt (claim 27) and the other components are not treated. Given the teachings of Petre, one of ordinary skill would have recognized that any components of the multivalent vaccine could be adsorbed, depending on the stability required/desired for each component. This is demonstrated by the fact that Petre teaches that other antigens (besides HBsAg) can be adsorbed or not adsorbed onto aluminum salt (claims 6, 7 and 27). Petre teaches amounts of antigens to be used in a 0.5 ml dose of a bulk vaccine, which can be optionally amended to use higher or lower quantities of the active ingredients: 10 μg HBsAg, 25 Lf diphtheria, 10 Lf tetanus, 25 μg of inactivated pertussis toxin, and 25 μg filamentous hemagglutinin (FHA), (page 11-12, examples 3 and 4). Petre differs from the claimed invention by not reciting the specific types of inactivated poliovirus antigens, types 1-3 (instant claims 33-35), although Petre does teach the use of inactivated poliovirus. Petre also differs from the claims invention by not reciting all of the amounts of antigenic elements of the instantly claimed vaccine (instant claims 33-35). The amounts of antigens in the claimed combined vaccine are: 30 Lf diphtheria, between 20-50 D antigen units of poliovirus type 1, between 4-10 D antigen units of poliovirus type 2, between 8-40 antigen units of poliovirus type 3, 10 μg HiB, 5 μg HBsAg, 20 μmoles of phosphates, 5 μmoles of carbonates, 0.125 ml of 50 μmolar tris buffer, and 0.356 mg aluminum salt.

However, Arminjon teaches a stable, multi-component vaccine comprising 10 μg of PRP-T (10 μg of HiB conjugated to tetanus toxoid), 1 vaccinating dose of diphtheria, 1 vaccinating

dose of tetanus, 15 μmoles of phosphates or 20 μmoles of carbonates, 0.25-0.3 mg of aluminum hydroxide, 40 U of polio antigen type I, 8 U of polio antigen type II, 32 U of polio antigen type III, 25 μg of pertussis anatoxin, 25 μg pertussis FHA, and 0.125 ml of 50 μmolar tris buffer (pages 2-3, and examples 12 and 13). Arminjon discusses the immunogenic instability of HiB (also referred to as PRP) coupled to tetanus anatoxin. (Note: Tetanus anatoxin is synonymous with tetanus toxoid. PRP-T is an abbreviation for HiB coupled to tetanus toxoid). Arminjon teaches that the PRP-T should be suspended in a solution containing anions (phosphate or citrate) prior to contacting them with aluminum complexes (page 6, lines 33-40). It would have been obvious to combine the teachings of Arminjon including polio virus antigens types 1-3, the specific amounts of antigens, and the amounts of phosphates, carbonates and aluminum salt from the teachings of Arminjon, with Petre's combined vaccine that comprises the antigenic elements of the claimed invention to arrive at the claimed invention. One would have been motivated to incorporate the teachings of Arminjon into Petre's vaccine because both references teach multi-component vaccine comprising antigens adsorbed to aluminum salts for stability purposes. Although Petre fails to teach the poliovirus antigens types 1-3 and the specific amounts of antigens of the instant invention, one would have been motivated to incorporate the antigens from Arminjon into Petre's method because Arminjon's vaccine demonstrates that multi-component vaccines having antigens adsorbed to aluminum salts are stable and effective for immunization. One would have had a reasonable expectation of success that the antigens of Arminjon would have been successfully incorporated into Petre's vaccine because multi-component stable vaccines are known, as evidenced by Petre and Arminjon.

(11) Response to Argument

The claims are rejected under 35 U.S.C. 103(a) as being obvious over Petre et al (WO 93/24148) in view of Arminjon et al. (AU 708777 or WO 96/37222). (Note: When Arminjon is referred to, it is the reference AU 708777, the disclosure of which is identical to WO 96/37222).

DISCUSSION

Appellant argues that the cited art, alone and in combination, fails to teach or suggest each and every limitation of the claims on appeal, and it fails to provide the ordinary artisan with a reasonable expectation of success. Appellant argues that the cited fails to teach or suggest a vaccine composition, together with an aluminum salt adjuvant, made by combining the valencies of pertussis toxoid, filamentous hemagglutinin, tetanus toxoid, diphtheria toxoid, inactivated poliovirus and a HiB (*H. influenzae* type B) conjugate, according to the claimed method. Appellant submits that the cited art does not teach or suggest the particular methods and compositions comprising the particular antigens claimed.

Appellant's arguments have been considered but fail to persuade because all the valencies of the claimed vaccine composition and the particular method of making the vaccine are present in the prior art of record. Petre teaches multicomponent vaccines for infants comprising various antigens such as diphtheria, tetanus, pertussis (toxoid and filamentous hemagglutinin), hepatitis B surface antigen (HBsAg), IPV (inactivated polio virus) and HiB (*H. influenzae* type B), (abstract, and page 4, lines 10-36). Petre teaches that the components of the combined vaccine are adsorbed to AH (aluminum hydroxide) or AP (aluminum phosphate). The following excerpt is taken from Petre, "After allowing time for complete and stable adsorption of the respective

components, the different components are combined under appropriate conditions", page 9, lines 1-3 of Petre. Therefore, Petre clearly teaches adsorption prior to mixing with other components. Arminjon teaches a stable, multi-component vaccine comprising 10 μg of PRP-T (10 μg of HiB conjugated to tetanus toxoid), 1 vaccinating dose of diphtheria, 1 vaccinating dose of tetanus, 15 μmoles of phosphates or 20 μmoles of carbonates, 0.25-0.3 mg of aluminum hydroxide, 40 U of polio antigen type I, 8 U of polio antigen type II, 32 U of polio antigen type III, 25 μg of pertussis anatoxin, 25 μg pertussis FHA, and 0.125 ml of 50 mmolar tris buffer (pages 2-3, and examples 12 and 13). Arminjon discusses the immunogenic instability of HiB/PRP coupled to tetanus anatoxin. Arminjon says that the PRP-T should be suspended in a solution containing anions (phosphate or citrate) prior to contacting them with aluminum complexes (page 6, lines 33-40). With regard to the specific amount of HBsAg instantly claimed (5μg; claims 34 and 35), the Office notes that neither the specification nor Appellant's arguments assert or establish this amount to be in any way critical in that no reason for the specific amount being claimed was provided. In addition, the prior art recognizes that the amount of HBsAg can be varied in the multivalent vaccine compositions (Petre, page 11, line 3; Arminjon, page 15, example 13) with predictable effect: the greater HBsAg will produce a greater immune response. One skilled in the art would have therefore found it obvious to vary the amount of HBsAg in the vaccine of Petre to achieve the optimal immune response for the subject being vaccinated absent unexpected results.

Appellant argues that the ordinary artisan would not have had a reasonable expectation of success for combining all of the antigens of the present claims to arrive at a composition having efficacy for each of its constituents. Appellant points to newly submitted Exhibit A (Eskola, *J.*

Infectious Diseases 174:S302-5, 1996) which discusses the uncertainty the ordinary artisan faces when combining antigens regarding the expectation of interference between HiB, diphtheria, tetanus and pertussis antigens in a combined vaccine (antigenic competition). Appellant asserts that one cannot pick any random combination of antigens and expect that a resultant vaccine will confer seroprotection against each disease-associated antigen selected.

Newly submitted Exhibit A (Eskola, *J. Infectious Diseases* 174:S302-5, 1996) has not been considered because exhibits submitted after a case has been appealed will not be admitted without a showing of good and sufficient reasons why they were not earlier presented (see 37 CRF § 1.195). The Office will address the arguments presented by Appellant without specific reference to the new exhibit.

Appellant's arguments have been considered but fail to persuade because the prior art shows that combined vaccines are effective to immunize against all their disease-related antigenic components. Arminjon shows that combined vaccines comprising PRP-T (HiB conjugated to tetanus toxoid), diphtheria, tetanus, polio antigens, pertussis toxoid, pertussis filamentous hemagluttinin and HBsAg (hepatitis B surface antigen) are useful as immunizations for infants (examples 12 and 13). Even if there was antigenic competition in Arminjon's combined vaccine, Arminjon's combined vaccine is evidence that multiple antigenic components can be combined into a vaccine and used for immunization.

Appellant also argues that since the Petre and Arminjon references are silent on antigenic competition, one would not have had a reasonable expectation of success that Appellant's combined vaccine would not exhibit antigenic competition. Appellant points to their

specification which discusses that the invention's combined vaccine's efficacy for conferring protection is surprising with respect to an expected antigenic competition effect.

Appellant's arguments have been considered but fail to persuade because the prior art shows that combined vaccines that contain multiple antigens confer protection. Even though Petre and Arminjon are silent on the subject of antigenic competition, their combined vaccines were successful for immunizing against disease-related antigens. While Appellant's disclosure discusses the surprising results of their combined vaccine, Petre and Arminjon have already demonstrated that combined vaccines immunize against their individual disease-related antigenic components. Despite the expectation of antigenic composition, the prior art's combined vaccines confer protection. Therefore, Appellant's asserted unexpected results are not unexpected because of the protection conferred by the prior art's combined vaccines.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

SBC

Examiner Stacy B. Chen
June 2, 2004

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